REMARKS

Claims 1, 3, 5, 10, 11, 13, 14 and 15 as amended are present for purposes of prosecution.

Claims 17 to 19 are withdrawn from prosecution as being directed to a non-elected invention.

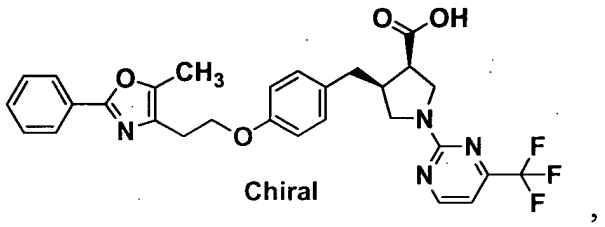
Specification

As requested by the Examiner, the abstract of the disclosure has been amended so that it contains less than 25 lines.

Election/Restrictions

The Examiner has required restriction to one of the following inventions as required under 35 U.S.C. §121:

I. Claims 1 to 16 (in part), drawn to compounds, compositions and a method of use wherein the ring defined by X_2-X_6 is defined in Example 170



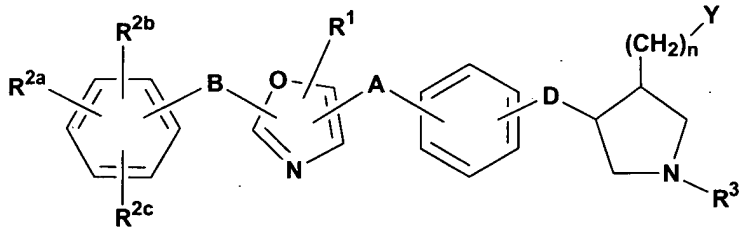
Q is C, X is CH, X^5 is 0, E, and Z^1 and Z^2 are carbon, classified in class 548 subclass 215.

II. Claims 1 to 16 (in part), drawn to compounds, compositions not contained in Group I, classified in various subclasses of class 544, 546, and 548 depending on the variables.

III. Claims 17 to 19 drawn to a pharmaceutical combination comprising a compound as defined in Claim 1 and a second agent, classified in various subclasses of 544, 546, and 548 depending on the variables.

Applicants, in a telephone election, elected for prosecution the compound of Example 170 as set out above.

Applicants elect Group I Claims 1 to 16 (in part). Thus, the elected compounds will have the structure



The claims have been amended to cover the elected compounds of Group I.

Claims 1 to 10, and 14 to 16 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The Examiner contends that:

> "The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following reasons apply:
>
> **Regarding the compounds and compositions of these claims**
>
> The nature of the invention in the instant application has claims that embrace a diversity of chemically and physically distinct compounds, wherein the core structure is substituted by R^3. While several compounds are disclosed, there is insufficient guidance for preparing all of the compounds embraced by the full scope of these claims, specifically, where R^3 can be arylalkyl broadly, arylcarbonyl broadly, heteroaryl broadly, heteroarylcarbonyl broadly, etc.; the full scope of which is found on page 527 of the claims.
>
> Furthermore, all compounds embraced by this broad scope have not been tested using the in vitro assays described in the specification. There is no data to support a conclusion of their effectiveness in treating diabetes, or any other blood glucose, triglyceride, insulin or NEFA modulating disease. Examples should be of sufficient scope as to justify the scope of the claim. However, the generic claims are much broader in scope than is represented by the testing. The definitions of the various R^3 variables on the substituted heterocyclic ring system embrace many structurally divergent groups not represented at all in testing, since testing for the instant compounds is not seen in the specification. Markush claims must be provided with support in the disclosure when the 'working examples' fail to include written

description(s) which teach how to make and use Markush members embraced thereby in full, clear and exact terms. See *In re Fouch, 169 USPQ 429.*

> This area of activity can be expected to be highly structure specific and unpredictable, as is generally true for chemically based pharmacological activity. In view of the structural divergence in the claims, one skilled in the art could not reasonably extrapolate the activities of some of the claimed compounds to the other structurally divergent compounds which are being used for their physiological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. *See In re Surrey 151 USPQ 724* regarding sufficiency of disclosure for a Markush group. No reasonable assurance has been made that the instant compounds as an entire class have the required activities needed to practice the invention, e.g. treat diabetes and related diseases. Thus, factors such as 'sufficient working examples,' 'the level of skill in the art,' and 'predictability in the art' have been demonstrated to be sufficiently lacking in the instant case for the scope being claimed."

Applicants submit that Claims 1, 3, 5, 10, 14 and 15, as amended, the claims remaining from the objected to Claims 1 to 10 and 14 to 16, are in compliance with 35 U.S.C. §112. Claims 1, 3, 5, 10, 14 and 15 as amended clearly contain subject matter which is described in the specification so as to enable one skilled in the art to make and use the invention.

Applicants' specification clearly defines the invention as now claimed.

Regarding the compounds claimed in Claims 1, 3, 5 and 10, the specification sets out 41 reaction schemes and a description of such schemes running from pages 17 to 78 of the specification as to how to make the compounds claimed. This disclosure sets out processes for preparing all compounds covered by the claims. In addition, the specification contains 488 real working examples for making compounds claimed. Thus, the specification clearly and unequivocally teaches how to make the compounds claimed.

In addition, the specification clearly teaches one skilled in the art how to use the compounds claimed. Please note pages 15 to 17 which clearly set out the disease states to be treated by the compounds of the invention. In addition, please note pages 106 and 107 of the specification which describes dosage forms containing the compounds claimed, the patients to be treated, the dosages to be employed and typical formulations. Thus, the specification clearly teaches one skilled in the art how to use the compounds claimed.

Please note that Claim 1 has been amended with respect to the R^3 substituent to cover compounds containing those R^3 substituents that are represented in the working examples or are

related to R^3 substituents represented in the working examples. Please refer to the working examples which disclose preparation of compounds as follows:

Example No.	R^3
1	arylalkyl
2	alkyloxycarbonyl
3	aryloxycarbonyl
4	aryl
36	alkoxyarylalkyl
47	heteroaryl
48 et seq.	various substituted heteroaryls
60, 61, 68 et seq.	substituted aryloxycarbonyls
159	arylsulfonyl
160, 163	alkylaminocarbonyl
164	arylheteroaryl
165	nitroheteroaryl
176	alkylcarbonylalkylcarbonyl
182	substituted aminocarbonyl
183	alkylcarbonyl
184	arylalkyloxycarbonyl
200	alkenyloxycarbonyl
208	alkoxycarbonylaryloxycarbonyl
209	alkoxyalkyloxycarbonyl
211	alkynyloxycarbonyl
217	carboxyaryloxycarbonyl
220	H
223	arylaminocarbonyl
228	aryl(alkyl)aminocarbonyl

Please note that the Examples generally cover compounds where R^3 is substituted arylalkyl, substituted alkoxycarbonyl, substituted aryloxycarbonyl, substituted heteroaryl, substituted aminocarbonyl, substituted alkenyloxycarbonyl, substituted sulfonyl, substituted oxycarbonyl. Thus, a number of the R^3 substituents remaining in Claim 1 may not specifically be covered in Examples 1 to 488. However, it will be apparent to those skilled in the art that compounds containing such substituents may be prepared as described in the reaction schemes and as described in the working examples and may be used to treat disease as described in the specification and mentioned hereinbefore.

It is not necessary that every last detail of an invention be described, by working examples or otherwise. Ex parte Wolters et al. (POBA 1979) 214 USPQ 735. Applicants need not provide a specific example of everything embraced by a broad claim. In re Anderson (CCPA 1973) 176 USPQ 331.

Applicants' specification clearly shows how to make and use the compounds now claimed. It is submitted that in view of the above, the Examiner has the burden of providing arguments why the specification as whole is not enabling. In re Morehouse (CCPA 1976) 192 USPQ 29.

The Examiner has the burden of showing that the disclosure entails undue experimentation. In re Angstadt (CCPA 1976) 190 USPQ 214. The Examiner has not advanced any valid reason or authority for doubting utility of Applicants' compounds as claimed other than broad sweeping statements of general applicability to any pharmaceutical application.

Applicants' compounds have similarities in structure to the compounds claimed in U.S. Patent No. 6,414,002 (copy enclosed) which teaches compounds useful for treating diabetes and related diseases.

Applicants' specification states that the compounds as disclosed and claimed are useful in treating diabetes and related diseases. In view of the disclosure in U.S. Patent No. 6,414,002, the Examiner has no valid grounds for doubting Applicants' statement of utility. In view of U.S. Patent No. 6,414,002, Applicants' assertions of usefulness and utility are believable on their face and straightforward. The Examiner has not advanced any reason or authority for doubting Applicants' statement of utility. Therefore, Applicants' disclosed utility must be accepted as accurate. In re Gazave (CCPA 1967) 154 USPQ 92.

The use of Applicants' compounds as claimed for treating diabetes and related diseases is not a speculative or incredible utility and cannot be validly challenged in view of the teachings in U.S. Patent No. 6,414,002. Applicants' compounds for use in treating diabetes is not in a field of endeavor which little of a successful nature has been developed. Applicants' statement of utility is credible in light of contemporary knowledge in the field of diabetes treatments (as evidenced by U.S. Patent No. 6,414,002) and thus need not be substantiated by evidence or testing.

In this regard, please also note U.S. Patent No. 6,875,782, WO 00/64888, U.S. Patent No. 6,635,655, WO 00/64876, U.S. Patent No. 5,939,442, and WO 98/00137, which disclose compounds which are useful for treating diabetes and related diseases and many of the references cited in Applicants' IDS which represent contemporary knowledge in the field of diabetes treatments.

Regarding Applicants' Markush group for R^3 defined in Claim 1, each member of the group is specifically contemplated in the specification and the Markush group for R^3 is supported by generic teaching, reaction schemes and examples which teach how to prepare these members and how to use compounds containing these members. The Examiner has not advanced any reason why all of the compounds of the claimed genus will not have the properties ascribed to them. Under these circumstances the Applicants' Markush group for R^3 should be acceptable although not every member of the group may be supported by a specific example directed thereto. Ex parte D'Alelio (POBA 1962) 137 USPQ 603, Ex parte Druey et al. (POBA 1964) 145 USPQ 219.

In view of the foregoing, it is submitted that Applicants' invention as claimed in Claims 1, 3, 5, 10, 14 and 15 are in compliance with 35 U.S.C. §112, first paragraph.

Regarding the methods of use defined in Claims 15 and 16, Claim 16 has been cancelled.

With regard to Claim 15, all diseases set out relate to diabetes and related diseases. As indicated above, in view of the contemporary knowledge regarding diabetes and related diseases (Claim 15 has been amended to delete inflammation) and the various references cited above which disclose compounds for use in treating diabetes, it is submitted that Applicants' method of use defined in Claim 15 should be accepted on its face and does not require undue experimentation.

Regarding Claims 15 and 16, the Examiner points out that the phrase "such as" renders the claim indefinite. Claim 15 has been amended to delete "such as".

Claims 6 to 10 and 13 are objected to for various minor informalities.

Claims 6 to 9 have been cancelled.

Claim 10 has been amended to delete a period in the middle of the claim as suggested by the Examiner.

Claim 13 has been amended to include a period, commas between each compound and the phrase such as "selected from the group consisting of...." before the first compound, and the word "and" is included before the last representative compound, as suggested by the Examiner.

The above amendments obviate the minor informalities in the claims.

In view of the foregoing, it is submitted that Claims 1, 3, 5, 10, 11, 13, 14 and 15 as present and amended are in compliance with 35 U.S.C. §112 and are in condition for allowance.

Respectfully submitted,

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000

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Burton Rodney
Attorney for Applicants
Reg. No. 22,076
Phone: 609-252-4336